ASX ANNOUNCEMENT

VivaGel® Study Demonstrates Reduced Risk of Recurrent BV

KEY POINTS:

- *1% VivaGel® demonstrated reduced risk of recurrent BV and delayed time to first recurrence in a Phase 2 study*
- *Several efficacy measures employed; all showed reduced risk with 1% VivaGel®*
- *More than 80% of 1% VivaGel® users remained BV free at 16 weeks*
- *High levels of patient satisfaction with VivaGel®*
- *VivaGel® was safe and well tolerated by trial participants over the 16 week treatment period*
- *Results strongly support progression to pivotal Phase 3 studies following input from FDA and other regulatory authorities*

Melbourne Australia; 3 April 2013 – Starpharma Holdings Ltd (ASX:SPL; OTCQX:SPHRY) today announced the positive results of its exploratory Phase 2 study of VivaGel® for the prevention of recurrent bacterial vaginosis (R-BV). The results showed a reduced overall risk of R-BV during the study in patients using 1% VivaGel® and time to first recurrence was delayed compared with placebo.

The results demonstrated the ability of VivaGel® to inhibit BV recurrence, as was suggested by results of earlier clinical trials, and they provide strong support for the advancement to Phase 3 clinical trials of VivaGel® for the prevention of R-BV.

"We are very pleased with these Phase 2 results. We have seen consistently lower recurrence rates with VivaGel® by every measure and these clinically relevant findings, if replicated in an appropriately designed larger Phase 3 study, would yield a positive pivotal result," said Starpharma Chief Executive Officer Dr Jackie Fairley.

"The commercial opportunity for recurrent BV is very attractive with an estimated market of more than $1 billion and following these results we have a high degree of confidence to move this product forward into Phase 3 clinical trials," Dr Fairley added.

To put these results into context, if the risk reduction results seen with 1% VivaGel® were applied more generally to all women with BV using published incidence data it is estimated that this would translate to the prevention of more than 10 million cases of R-BV annually in the US alone.

The Phase 2 study also showed high levels of user satisfaction, in line with earlier clinical trials of VivaGel®. In this study 79% of users of 1% VivaGel® were either satisfied, very satisfied or extremely satisfied with the product's effectiveness and overall satisfaction.

In the study, 205 women were randomised to VivaGel® containing either 1% or 3% SPL7013, or placebo following a course of conventional BV treatment (metronidazole). Women used the product every second day for 16 weeks. The primary objective of the study was to assess the efficacy of VivaGel® in reducing the risk of R-BV compared with placebo.

As an exploratory, dose ranging Phase 2 study for a new indication with no approved treatments, a number of different efficacy measurements were undertaken at various time points with a view to identifying the most appropriate endpoints and trial design for Phase 3 studies. The primary clinical endpoint of recurrence of BV was assessed during the 16 week treatment period. The following criteria were used to diagnose R-BV, either alone or in combination:

1. the presence of clinical signs (Amsel criteria) as assessed by the investigator;
2. the presence of BV symptoms reported by the patients; and
3. the investigator's own determination as to whether the patient had BV.

Summary of Results and Commentary

Detailed results are shown in the Appendix to this announcement.

By all efficacy measures, patients treated with 1% VivaGel® demonstrated a reduced risk of recurrent BV compared with placebo. The 1% VivaGel® group also had a delayed time to first recurrence of BV with more than 80% of VivaGel® users remaining BV free at 16 weeks.

When R-BV was determined by the presence of three of the most clinically important Amsel criteria, as stipulated by FDA (abnormal discharge, whiff test and presence of clue cells), the risk of R-BV was reduced in the 1% VivaGel® group (12%) compared with both the 3% VivaGel® (23%) and placebo groups (28%). This difference represents a relative risk reduction in R-BV with 1% VivaGel® of 56% compared with placebo at the end of 16 weeks. Using these key criteria, the difference between 1% and placebo groups was close to statistically significant (P=0.0588).

When assessed according to a combination of criteria (i.e. presence of patient-reported BV symptoms and at least 3 Amsel criteria), the risk of R-BV was again shown to be reduced in the 1% VivaGel® group (17%) compared with both the 3% VivaGel® (26%) and placebo groups (28%). This difference represents a clinically significant relative risk reduction in BV

recurrence of 39% with 1% VivaGel® compared with placebo, but by this measure the difference was not statistically significant.

Commenting on the trial results, expert clinical advisor to the program, Professor George Kinghorn, OBE, Clinical Director at NIHR Clinical Research Network, Department of Genitourinary Medicine, Royal Hallamshire and Sheffield Teaching Hospitals in the UK, said:

"As a clinician, I am very encouraged by the data for 1% VivaGel®. In this group of women, almost all would have been expected to experience recurrent BV during the study. However, more than 80% of VivaGel® users remained BV free at 16 weeks. Given there are no other approved products for recurrent BV, I see this finding as highly promising – both for the management of women with this often difficult chronic condition and for recurrent BV sufferers."

The time to the first case of R-BV in the patients using 1% VivaGel® was 35 days, while in the patients using placebo, the first case of R-BV occurred after just 5 days. At the Week 4 visit, the relative risk reduction of R-BV with 1% VivaGel® was 77% compared with placebo, and this reduction was close to statistically significant (P= 0.0729, or 0.0489 when one patient with unknown R-BV status in each group was excluded).

The data also showed that the rate of recurrence in the placebo group reached 20% between weeks 4 and 8 of the study, while the rate of recurrence in the 1% VivaGel® group reached 20% only after cessation of treatment beyond week 16. Furthermore, the proportion of women with BV symptoms of discharge and/or odour at the Week 16 visit was approximately 4-times lower in the 1% SPL7013 Gel group compared with placebo (4% vs. 17%) (P=0.0803). In addition to R-BV, these data also feed into the symptomatic relief strategy currently being explored in parallel for VivaGel®.

In a subgroup of women enrolled in the study, who had BV confirmed by presence of a Nugent score of 4-10 at Screening, time to R-BV was increased in the 1% VivaGel® group compared with placebo at the end of the 16 week treatment period, and even with the reduced number of women in this subgroup this difference came close to statistical significance at the 0.05 level (P=0.0598).

In addition, at each of the 4-weekly visits during treatment (Weeks 4, 8, 12 and 16), the number of women who reported experiencing BV signs and symptoms since their last visit was consistently lower in the 1% VivaGel® group compared with placebo. This difference was statistically significant at Week 4 (9% vs. 23%, P=0.0434) and Week 16 (2% vs. 14%, P=0.0507).

In the follow-up period, once use of study product stopped, there was no difference in the proportion of women in the 1% SPL7013 Gel and placebo groups reporting BV symptoms, indicating that the product concept, ie. on-going use of VivaGel®, would be beneficial in reducing recurrence of BV symptoms.

The rate of adverse events in the 1% VivaGel® group was comparable with placebo, and significantly lower than published data on metronidazole when used for extended periods of time. The rate of candidiasis (19%) was also very low compared with that reported following long-term use of metronidazole (44%).[1]

[1] Sobel et al, 2006

In general, 1% VivaGel® performed best compared with placebo, while in general the 3% dose did not reduce the risk of R-BV. These clinical findings correlate with the earlier Phase 2 dose ranging results and *in vitro* microbiological findings, which show that 1% SPL7013 achieves the best balance between activity against pathogenic BV bacteria and the beneficial *Lactobacillus* species. These findings will be further explored including the observation that there was a higher level of patient drop-outs in the 3% group prior to the first post-baseline study visit at Week 4 (19%) compared with 1% group (4% drop-out) and placebo (11% drop-out). Given the very early drop-out of these participants, and the very good safety profile of all products throughout the remainder of the study, it did not appear that this discontinuation was associated with any product-related effects or adverse events.

This study demonstrated consistent and clinically significant reduced risk of R-BV in the 1% VivaGel® group and findings from this trial will prove invaluable to inform and optimise trial design parameters for pivotal Phase 3 studies. Given this was a relatively small, exploratory, dose ranging Phase 2 study for a new treatment where no other registered products exist, it is not unexpected that statistical significance would not be achieved on all efficacy measures. Statistical modelling indicates that if these results were replicated in an appropriately designed, larger Phase 3 study, it would yield a statistically significant result.

Next Steps

On the basis of these very encouraging results, planning for the conduct of a pivotal Phase 3 trial program for VivaGel® in R-BV has now commenced and discussions will be held in coming months with regulatory authorities, including the US FDA, on the most appropriate design of pivotal studies. These positive results will also be advantageous in progressing discussions with commercial partners which will continue in parallel with Phase 3 planning activities.

BV is the most common vaginal infection worldwide, and the most common cause of vaginal irritation, discharge and malodour. It is particularly prevalent in the US, where it affects an estimated one-third of the adult female population and up to 50% of the female population in some regions. Studies indicate as many as 50-60% of those women have recurrent episodes of BV.[2,3]

Existing treatments for BV are considered suboptimal with relatively low cure rates and high rates of recurrence, unpleasant side-effects, and high levels of bacterial resistance. There are no treatments currently on market for the prevention of recurrence of BV; however the market is estimated to be in excess of $1 billion.

[2] Marrazzo, 2011

[3] Bradshaw et al, 2006

ABOUT STARPHARMA

Starpharma Holdings Limited (ASX:SPL, OTCQX:SPHRY), located in Melbourne Australia, is an ASX 300 company and is a world leader in the development of dendrimer products for pharmaceutical, life science and other applications.

Starpharma's underlying technology is built around dendrimers – a type of synthetic nanoscale polymer that is highly regular in size and structure and well suited to pharmaceutical uses. Starpharma has three core development programs: VivaGel® portfolio, drug delivery, and agrochemicals with the Company developing a number of products internally and others via commercial partnerships.

Starpharma's lead product is VivaGel® (SPL7013 Gel), a gel-based formulation of a proprietary dendrimer. VivaGel® is under clinical development for the treatment and prevention of bacterial vaginosis (BV) and also as a vaginal microbicide to prevent the transmission of sexually transmitted infections including HIV and genital herpes. Starpharma has also signed separate licence agreements with Ansell Limited (ASX:ANN) and Okamoto Industries Inc (Tokyo Stock Exchange) to market a value-added, VivaGel®-coated condom. Ansell manufactures and sells leading condom brands worldwide, including Lifestyles®, ZERO® and SKYN®. Okamoto is the market leader for condoms sold in Japan, the world's second largest condom market.

In the wider pharmaceutical and life science fields, Starpharma has both partnered and internal programs in Drug Delivery. Drug Delivery partners include GSK, Lilly and AstraZeneca. In its internal program Starpharma has announced significant tumour-targeting results in its docetaxel (Taxotere®) program, with animal studies showing its dendrimer-enhanced version of docetaxel to have significantly superior anti-cancer effects across a range of important cancer types including breast, prostate, lung and ovarian tumour, when compared to Taxotere® (docetaxel).

In agrochemicals Starpharma has a series of partnerships with leading industry players including Nufarm (ASX:NUF) and Makhteshim Agan as well as internal programs including an enhanced version of glyphosate (the active ingredient in Roundup®).

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Forward Looking Statements

This document contains certain forward-looking statements, relating to Starpharma's business, which can be identified by the use of forward-looking terminology such as "promising", "plans", "anticipated", "will", "project", "believe", "forecast", "expected", "estimated", "targeting", "aiming", "set to", "potential", "seeking to", "goal", "could provide", "intends", "is being developed", "could be", "on track", or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA's and other health authorities' requirements regarding any one or more product candidates nor can there be any assurance that such product candidates will be approved by any health authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialization of the product candidates could be affected by, among other things, unexpected clinical trial results, including additional analysis of existing clinical data, and new clinical data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected. Starpharma is providing this information as of the date of this document and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise.

APPENDIX 1 – CLINICAL TRIAL SUMMARY

Official Title:	A double-blind, multicenter, randomized, placebo-controlled, dose-ranging study to determine the efficacy and safety of SPL7013 Gel (VivaGel®) administered vaginally to prevent the recurrence of bacterial vaginosis
Identifying Codes:	Starpharma Protocol Number: SPL7013-014
Primary Objective:	To assess the efficacy of 1% and 3% SPL7013 Gel, used every second day for 16 weeks, in reducing the rate of recurrence of bacterial vaginosis (BV) in subjects with a history of recurrent BV
Primary Endpoint:	The recurrence of BV by or at the End of Treatment visit (Week 16)
Secondary Objectives:	To determine the safety and tolerability of 1% and 3% SPL7013 Gel when used every second day for 16 weeks; To assess the acceptability of treatment with 1% and 3% SPL7013 Gel; and To characterise the distribution of times to recurrence of BV in subjects with a history of recurrent BV when treated with SPL7013 Gel every second day for 16 weeks (vs. placebo).
Study Design:	Randomised, double-blind, multicentre, placebo-controlled, dose-ranging study of women with active BV and a history of recurrent BV. Recurrent BV was defined as a history of at least 3 episodes of BV in the past 12 months, including the current episode. After Screening for BV, and receiving successful treatment with metronidazole for 7 days, eligible subjects were randomised at Baseline to receive 1% SPL7013 Gel, 3% SPL7013 Gel, or placebo gel every second day for 16 weeks, followed by an 8-week follow-up period without drug.
Sites:	The study was conducted at 10 sites in the US.
Key Inclusion Criteria:	• Female, aged 18 to 45 years • history of recurrent BV • current diagnosis of BV • otherwise healthy, as determined by medical history • normal Pap smear at or documented within 24 months of screening
RESULTS	
Demographics	A total of 205 participants, aged 18 to 45 years, were randomised to receive 1% SPL7013 Gel (N=68), 3% SPL7013 Gel (N=67) or placebo gel (N=70) (Intent to Treat (ITT) population). Groups were generally well-balanced with respect to characteristics at Screening including race, ethnicity, history of recurrent BV, smoking status, and Nugent score. The modified ITT (mITT) population consisted of all women in the ITT who had administered at least one dose of study medication and had at least one post-baseline efficacy evaluation. A total of 179 women formed the mITT in the 1% SPL7013 Gel (N=65), 3% SPL7013 Gel (N=53) and placebo groups (N=61). Unless stated otherwise, results quoted in this announcement relate to the mITT population.

Recurrence of BV: The rates of R-BV following the 16 week treatment period, according to four different combinations of criteria used in this study (R-BV definitions 1-4, see Table 1), are shown in Figure 1 and Table 1.

Figure 1.

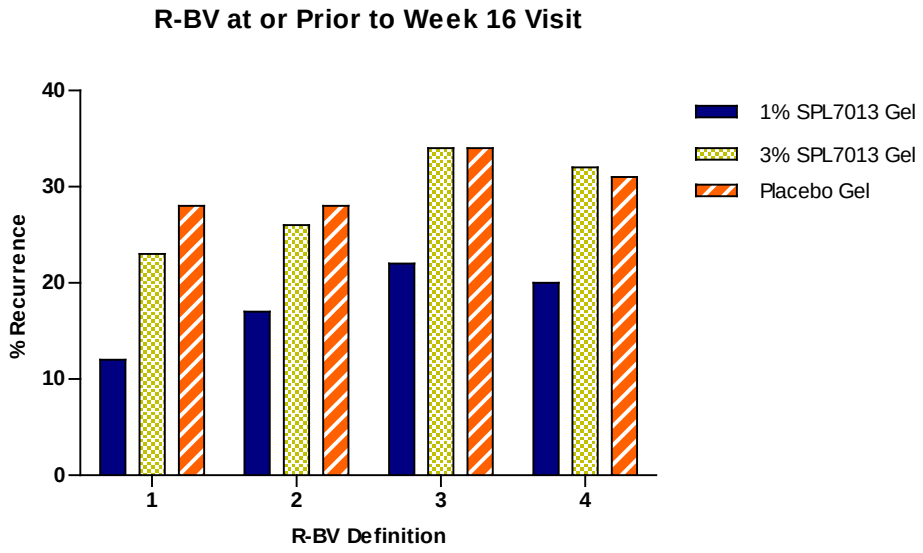


Table 1.

R-BV Def.	R-BV Criteria	Treatment			Relative Risk Reduction (1% SPL7013 Gel vs. Placebo)
		1% SPL7013 Gel (N=65)	3% SPL7013 Gel (N=53)	Placebo Gel (N=61)	
1	Amsel criteria (discharge, whiff, clue cells; i.e., FDA stipulated Amsel)	12%*	23%	28%	56%
2	Patient reported symptoms and at least 3 of the 4 Amsel criteria	17%	26%	28%	39%
3	At least 3 of the 4 Amsel criteria	22%	34%	34%	38%
4	Investigator's determination patient has BV	20%	32%	31%	36%

**P=0.0588*

The risk of R-BV was substantially reduced in the 1% SPL7013 Gel group according to all criteria assessed, and based on expert clinical input this level of relative risk reduction is considered to be clinically significant (Table 1). In the 1% SPL7013 Gel group, close to statistically significant reduced risk of BV was seen at week 16 when R-BV was assessed according to the three key Amsel criteria, as stipulated by FDA.

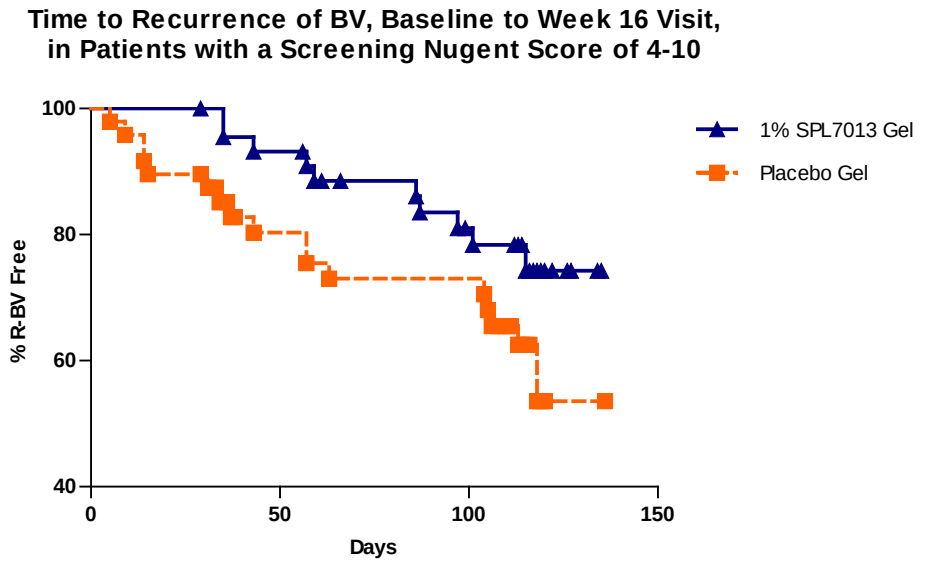
In addition to the finding at week 16, the risk reduction of R-BV was also assessed at weeks 4, 8 and 12 of treatment. The difference between rates of R-BV was close to or achieved statistical significance (1% SPL7013 Gel vs. placebo) at weeks 4 and 8 of treatment when the relative risk reduction with VivaGel® was as high as 77% (mITT and ITT populations) (see Table 2).

Table 2.

Analysis Population	Recurrence of BV at or Prior to Week 4			Recurrence of BV at or Prior to Week 8		
	Treatment		Relative Risk Reduction	Treatment		Relative Risk Reduction
	1% SPL7013 Gel	Placebo Gel		1% SPL7013 Gel	Placebo Gel	
ITT	*(N=68)* **3%** *P=0.0461*	*(N=70)* **11%**	**76%**	*(N=68)* **9%** *P=0.0660*	*(N=70)* **17%**	**49%**
mITT	*(N=65)* **3%** *P=0.0729*	*(N=61)* **13%**	**77%**	*(N=65)* **9%** *P=0.2135*	*(N=61)* **20%**	**53%**

In women with BV confirmed by presence of a Nugent score of 4-10 at Screening, the difference in time to recurrence of BV between the 1% SPL7013 Gel and placebo groups, as determined by survival curve analyses, was close to statistically significant (P=0.0598) (see Figure 2).

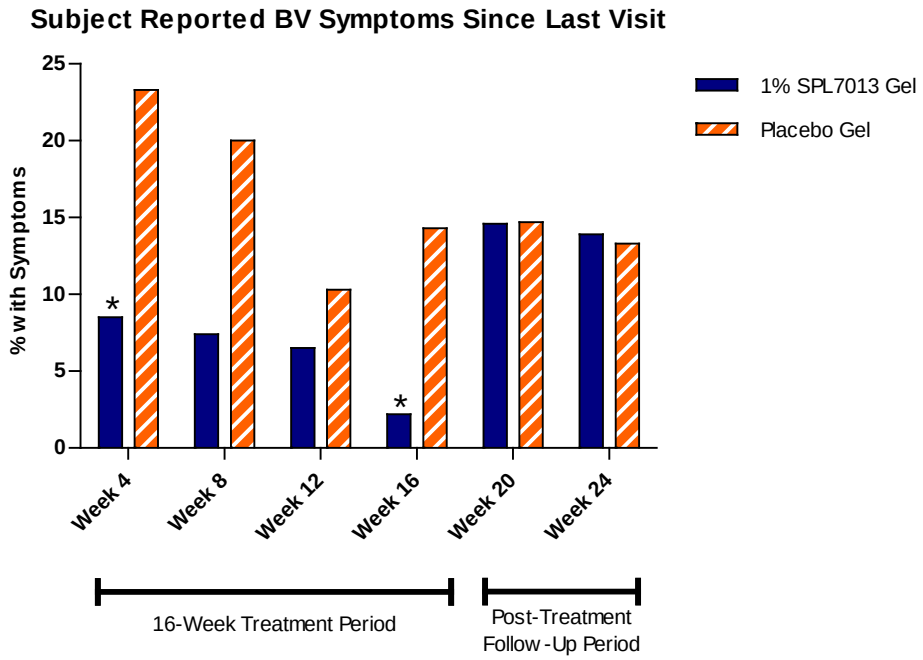
Figure 2.



Recurrence of BV Symptoms: The proportion of women with BV symptoms of discharge and/or odour at the Week 16 visit was almost 4-times lower in the 1% SPL7013 Gel group compared with placebo (4% vs. 17%) (P=0.0803).

In addition, at each of the 4-weekly visits during treatment (Weeks 4, 8, 12 and 16), the number of women who reported experiencing BV signs and symptoms since their last visit was consistently lower in the 1% SPL7013 Gel group compared with placebo (see Figure 3). This difference was statistically significantly different at Week 4 (9% vs. 23%, P=0.0434) and Week 16 (2% vs. 14%, P=0.0507). In the follow-up period (weeks 20 and 24), once use of study product stopped, there was no substantial difference in the proportion of women in the 1% SPL7013 Gel and placebo groups reporting BV symptoms.

Figure 3.



** Statistically significant (P ≤ 0.05) vs. placebo*

Acceptability: Patients rated the gels equally, and highly positively, in terms of convenience and side effects. The 1% SPL7013 Gel was rated highest in terms of effectiveness and global satisfaction. Overall, 79% of patients using the 1% SPL7013 Gel were satisfied, very satisfied or extremely satisfied, compared with 66% of patients using 3% SPL7013 Gel or placebo gel.

Treatment Compliance: Of the participants who returned study product applicators for drug accountability assessment, treatment compliance was 93% in the 1% SPL7013 Gel group compared with 79% in the 3% SPL7013 Gel group and 91% in the placebo group.

Safety: There were no deaths or serious adverse events (SAEs) during the study.

In general, the safety profile of SPL7013 Gels and placebo was comparable.

Overall, 53% of women in the 1% SPL7013 Gel, compared with 46% in the 3% SPL7013 Gel group and 41% in the placebo group experienced any adverse event (AE). In a similar published study of long term metronidazole, 82% of patients using that product for 16 weeks were reported to experience an AE.[1]

In the current study, 19% of women in the 1% SPL7013 Gel, compared with 18%

[1] Sobel et al, 2006.

in the 3% SPL7013 Gel group and 13% in the placebo group experienced any treatment-related AE.

Treatment-related genitourinary AEs were reported in 19% of women in the 1% SPL7013 Gel group, compared with 17% in the 3% SPL7013 Gel group and 13% in the placebo group.

Candidiasis was reported in 19% of women in the 1% SPL7013 Gel group, compared with 26% in the 3% SPL7013 Gel group and 15% in the placebo group. During treatment, 15% of women reported candidiasis in the 1% SPL7013 Gel group compared with 9% in placebo.

In the published study of metronidazole for 16 weeks referenced earlier, 44% of women using metronidazole for 16 weeks reported candidiasis. Overall, 59% of women using metronidazole in that study were prescribed antifungal treatment. In the current study, only 19% of participants in the 1% SPL7013 Gel group used antifungals. This finding in itself indicates the potential for greatly reduced patient medication and financial burden through use of VivaGel®, as opposed to conventional antibiotics, for prevention of R-BV.

Only one participant was reported to have discontinued the study due to an AE (in the 3% SPL7013 Gel group).